PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
I/98404 WO		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/EP 99/ 05476	26/07/1999	31/07/1998
Applicant		
AKZO NOBEL N.V. et. al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [ ] contained in the international application in written form.

   [ ] filed together with the international application in computer readable form.

   [ ] furnished subsequently to this Authority in written form.

   [ ] furnished subsequently to this Authority in computer readble form.

   [ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. 2

   [ ] as suggested by the applicant.

   [X] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

   [ ] None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 99/05476

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/38 C12N7/04 A61K39/245 A61K39/27

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12N A61K C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LEWIS JB ET AL: "Transcriptional control of the equine herpesvirus 1 immediate early gene" VIROLOGY, vol. 197 , no. 2 , December 1993 (1993-12), pages 788-792, XP002125016 ORLANDO US Plasmid pIEbetagal containing the EHV-1 Immediately Early promoter. page 788, right-hand column, last paragraph ---	7,8
A	WO 92 01045 A (THE UNIVERSITY OF GLASGOW) 23 January 1992 (1992-01-23) example 3 --- -/--	1-8, 10-12

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
8 December 1999	18/01/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Cupido, M

1

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 99/05476

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	SMITH R H ET AL.: "Nuclear localization and transcriptional activation activities of truncated versions of the Immediate-Early gene product of Equine Herpesvirus 1" JOURNAL OF VIROLOGY, vol. 69, no. 6, June 1995 (1995-06), pages 3857-3862, XP002088567 the whole document	1-17
A	MARSHALL K R ET AL: "AN EQUINE HERPESVIRUS-1 GENE 71 DELETANT IS ATTENUATED AND ELICITS A PROTECTIVE IMMUNE RESPONSE IN MICE" VIROLOGY,US,ACADEMIC PRESS,ORLANDO, vol. 231, no. 1, page 20-27 XP002055348 ISSN: 0042-6822 EHV-1 gene 71 deletion mutant is attenuated and may be used as vaccine strain (see also WO98/26049) the whole document	1-17
A	WO 96 04394 A (MEDICAL RESEARCH COUNCIL) 15 February 1996 (1996-02-15) page 5, line 15 -page 6, line 25	15-17

1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/EP 99/05476

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9201045 A	23-01-1992	AU 8212891 A	04-02-1992
		CA 2086740 A	07-01-1992
		EP 0538299 A	28-04-1993
		HU 67778 A	28-04-1995
		NZ 238834 A	26-05-1992
WO 9604394 A	15-02-1996	AU 695405 B	13-08-1998
		AU 3119595 A	04-03-1996
		CA 2195965 A	15-02-1996
		EP 0804602 A	05-11-1997
		JP 10503372 T	31-03-1998

PATENT COOPERATIO.. TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 29 March 2000 (29.03.00)	
International application No. PCT/EP99/05476	**Applicant's or agent's file reference** 1/98404 WO
International filing date (day/month/year) 26 July 1999 (26.07.99)	**Priority date** (day/month/year) 31 July 1998 (31.07.98)
Applicant SONDERMEIJER, Paulus, Jacobus, Antonius et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

25 February 2000 (25.02.00)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

F. Baechler

Telephone No.: (41-22) 338.83.38

PATENT COOPERAT... TREATY

From the INTERNATIONAL BUREAU

PCT

COMMUNICATION IN CASES FOR WHICH NO OTHER FORM IS APPLICABLE

To:
OGILVIE-EMANUELSON C., M.
P.O. Box 20
NL-5340 BH Oss
PAYS-BAS

Date of mailing (*day/month/year*) 13 February 2001 (13.02.01)	
Applicant's or agent's file reference 1/98404 WO	**REPLY DUE** see paragraph 1 below
International application No. PCT/EP99/05476	International filing date (*day/month/year*) 26 July 1999 (26.07.99)
Applicant AKZO NOBEL N.V.	

1. ☐ REPLY DUE within _____ months/days from the above date of mailing

☐ NO REPLY DUE, however, see below

☒ IMPORTANT COMMUNICATION

☐ INFORMATION ONLY

2. COMMUNICATION:

It has been brought to the attention of the International Bureau (WO) that in respect of the above-identified application, the international publication No. WO 00/08165 mailed on 17 February 2000 indicated the priority country code NL instead of EP.

The International Bureau shall publish a correction is Section II of the PCT Gazette. A corrected version of the pamphlet will be published on that same day.

A copy of this Notification has been sent to the receiving Office (RO/EP) and to the elected Offices concerned.

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer
Maria Victoria CORTIELLO

Telephone No. (41-22) 338.83.38

4T
09/744799
Translation
0520

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference NP-1669W	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/JP99/04308	International filing date (*day/month/year*) 10 August 1999 (10.08.99)	Priority date (*day/month/year*) 10 August 1998 (10.08.98)
International Patent Classification (IPC) or national classification and IPC A61K 31/375, A61P 29/00 // C07D 307/62		
Applicant NIPPON HYPOX LABORATORIES INC.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 3 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
25 November 1999 (25.11.99)	02 August 2000 (02.08.2000)
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/JP99/04308

I. Basis of the report

1. With regard to the **elements** of the international application:*

☐ the international application as originally filed

☒ the description:

pages 1-18, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☒ the claims:

pages _____, as originally filed
pages 2-4, as amended (together with any statement under Article 19
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the drawings:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the sequence listing part of the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☒ the claims, Nos. 1
☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/JP99/04308

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	2-4	YES
	Claims		NO
Inventive step (IS)	Claims	2-4	YES
	Claims		NO
Industrial applicability (IA)	Claims	2-4	YES
	Claims		NO

2. Citations and explanations

Documents cited in the ISR:
Document 1: JP, 44-27224, B
Document 2: JP, 62-87509, A
Document 3: JP, 2-209807, A
Document 4: JP, 57-24308, A
Document 5: JP, 9-12450, A

None of the documents cited in the ISR disclose the compounds of the present application in which the 3 position of ascorbic acid is substituted with an alkyl group, an alkylcarbonylmethyl group or an alkoxycarbonylmethyl group. Moreover, it is acknowledged that, as stated in the test report submitted with the written reply, said 3-O-substituted compounds exhibit remarkable effects in terms of stability and safety. It is thus considered that the subject matter of claims 2-4 is both novel and involves an inventive step.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
1/98404 WO		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP99/05476	26/07/1999	31/07/1998
International Patent Classification (IPC) or national classification and IPC C12N15/38		
Applicant AKZO NOBEL N.V. et. al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
25/02/2000	10.11.2000
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Armandola, E Telephone No. +49 89 2399 7493

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP99/05476

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).)*:
Description, pages:

1-15	as originally filed				

Claims, No.:

1-15	as received on	06/09/2000	with letter of	05/09/2000	

Drawings, sheets:

1/2,2/2	as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   ☐ the language of publication of the international application (under Rule 48.3(b)).
   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.
   ☐ filed together with the international application in computer readable form.
   ☐ furnished subsequently to this Authority in written form.
   ☐ furnished subsequently to this Authority in computer readable form.
   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:
   ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	6-10, 13-15
	No:	Claims	1-5, 11, 12
Inventive step (IS)	Yes:	Claims	6-10, 13-15
	No:	Claims	1-5, 11, 12
Industrial applicability (IA)	Yes:	Claims	1-15
	No:	Claims	

2. Citations and explanations
   see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following document:

D1: LEWIS JB ET AL: 'Transcriptional control of the equine herpesvirus 1 immediate early gene' VIROLOGY, vol. 197 , no. 2 , December 1993 (1993-12), pages 788-792, XP002125016 ORLANDO US

D2: ELLIOT G AND O'HARE P: 'Equine herpes virus 1 gene 12, the functional homologue of herpes simplex virus VP16, transactivates via octamer sequences in the equine herpesvirus IE gene promoter.', VIROLOGY,1996, vol. 213, pages 258-262

D3: WO 92 01045 A (THE UNIVERSITY OF GLASGOW) 23 January 1992 (1992-01-23)

D4: MARSHALL K R ET AL: 'AN EQUINE HERPESVIRUS-1 GENE 71 DELETANT IS ATTENUATED AND ELICITS A PROTECTIVE IMMUNE RESPONSE IN MICE' VIROLOGY,US,ACADEMIC PRESS,ORLANDO, vol. 231, no. 1, page 20-27 XP002055348 ISSN: 0042-6822

Document D1 discloses the plasmid plEbetagal containing the EHV-1 Immediate Early promoter.

Document D2 discloses a nucleic acid sequence comprising EHV-1 IE promoter and deletion mutants thereof. This nucleic acid sequence is enclosed in a vector and is transfected into host cells.

Document D3 describes an attenuated EHV-4 vaccine comprising an EHV-4 mutant.

Document D4 reports the creation of an attenuated mutant of HEV-1 by deletion of sequences in the coding region of gene 71 (EUS4) and of its usefulness in eliciting a protective immune response in mice.

Document D2 was not cited in the ISR.

Novelty (Art. 33(2) PCT)

i) In view of the unclear definition of their subject matter (see Item VIII), Claims 1-5, 11 and 12 cannot be considered novel. As no wild type reference (by means of e.g. its nucleotide sequence or access/deposit number) is provided, any EHV sequence can be considered as wild type or mutant. EHV isolates, vaccines and cells infected with EHV are known (see e.g. D3, D4).

ii) Claims 6-10 can be considered novel because an EHV-1 mutant comprising a deletion of the restriction fragments of the promoter region of the Immediate Early protein gene as described in the claims has not been disclosed in the prior art. Document D2 discloses mutants of the EHV-1 IE promoter but this is isolated and part of a cloning vector.

iii) Claims 13-15 can be considered novel because a method of genetically attenuating EHV by mutating the endogenous promoter region of an essential gene has not been disclosed in the available prior art.

Inventive step (Art. 33(3) PCT)

Claims 6-10 and 15-17 can be considered to entail an inventive step as their subject matter has not been rendered obvious in the prior art:
The mutants described in Claims 6-10 obtained by the deletion of specific restriction fragments in the promoter of the IE gene could not have been derived by the skilled person from the prior art without exercising inventive activity;
with regard to Claims 15-17, attenuated mutants of HEV-4 and HEV-1 mutant are described in D3 and D4, respectively. Both of these mutants are, however, deleted in the coding regions of genes and not in their promoters. In order to produce an attenuated virus mutant the skilled person would have found no indication in the prior art that might have led him/her to consider the deletion within a promoter sequence as a possible method to create such mutant with reasonable expectation of success.

Re Item VIII

Certain observations on the international application

The subject-matter of Claims 1-5, 11 and 12 is not sufficiently defined. As no consensus wild type sequence has been provided, any known EHV could be considered a mutant and could fall within the scope of the claims.

The mutant of Claim 1 is defined "with respect to the parent strain", this parent strain not being better identified (e.g. by its genomic sequence or access/deposit number etc.).

Viruses spontaneously mutate as they get transmitted from one host to the other. Of two isolates differing by point mutations, it would be hard to determine which one is the parent and which the mutant. The skilled person isolating EHV from a host, would not know if the isolate represents a mutant with respect to a parent strain or not, because he/she would not know to which parent strain to compare the isolate.

Moreover, the subject-matter of Claim 1 (and consequently of the dependent claims) encompasses spontaneous mutants which do not fall within the scope of the invention. This is due to the fact that one of the features which appear essential to the invention are missing from the claims, namely the feature that the mutant should display an attenuated virulence phenotype.

Therefore, any EHV isolate could prejudice the novelty of Claims 1-5, 11 and 12 (see also Item V).

CLAIMS

1. Equine herpesvirus (EHV) mutant, comprising one or more deletions, substitutions or insertions in the endogenous promoter region of an essential viral gene.
2. EHV mutant as claimed in claim 1, wherein deletions are introduced into the promoter.
3. EHV mutant as claimed in claims 1-2, wherein the gene is the Immediate Early gene.
4. EHV mutant as claimed in claims 1-3, wherein the mutant virus is the EHV-1 virus or the EHV-4 virus.
5. EHV mutant as claimed in claims 1-4, further comprising one or more mutations in one or more other genes and/or their promoters.
6. EHV-1 mutant as claimed in claims 1-5, comprising a deletion of the SacI-SacI fragment or the HindIII-ClaI fragment or the NdeI-NdeI fragment or the SphI-SphI fragment of the promoter region of the Immediate Early gene.
7. Nucleic acid sequence, comprising the endogenous promoter region of an essential gene from EHV and optionally one or more flanking sequences, which promoter region comprises one or more deletions, substitutions or insertions.
8. Nucleic acid sequence as claimed in claims 7, wherein the gene is an Immediate Early gene.
9. Nucleic acid sequence as claimed in claim 8, comprising a deletion of the SacI-SacI fragment or the HindIII-ClaI fragment or the NdeI-NdeI fragment or the SphI-SphI fragment of the promoter region of the Immediate Early gene.
10. Nucleic acid sequence as claimed in claims 7-9, wherein the EHV is EHV-1 or EHV-4.
11. Recombinant DNA molecule comprising a nucleic acid sequence as claimed in claims 7-10.
12. Host cell harbouring a recombinant DNA molecule as claimed in claim 11.
13. Vaccine comprising an EHV mutant as claimed in claims 1-6 and a pharmaceutically acceptable carrier or diluent.
14. A process for the preparation of an EHV mutant as claimed in claims 1-6, comprising transfecting a cell culture with a recombinant DNA molecule as claimed in claim 11 and EHV genomic DNA.

15. Method of genetically attenuating EHV, comprising mutation of the endogenous promoter region of an essential gene, which mutation consists of one or more deletions, substitutions or insertions in the promoter region of an essential gene.

16. Method as claimed in claim 15, wherein the EHV is EHV-1 or EHV-4.

17. Method as claimed in claims 16-17, wherein the gene is an Immediate Early gene.